

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International BureauINTERNATIONAL² APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification⁵ : A61K 31/74	A1	(11) International Publication Number: WO 94/09796 (43) International Publication Date: 11 May 1994 (11.05.94)
(21) International Application Number: PCT/US93/09869 (22) International Filing Date: 13 October 1993 (13.10.93) (30) Priority data: 965,641 23 October 1992 (23.10.92) US 130,113 6 October 1993 (06.10.93) US (71) Applicant: ABBOTT LABORATORIES [US/US]; One Abbott Park Road, Abbott Park, IL 60064-3500 (US). (72) Inventors: SIBLEY, Murray, Jack ; 4999 Deer Forest Place, Westerville, OH 43081 (US). HARTUNG, Donald, Ernest ; 519 South Lincoln Lane, Arlington Heights, IL 60005 (US). RULAND, Rosalyn ; 2787 Bellwood Avenue, Bexley, OH 43209 (US).		(74) Agents: DRAYER, Lonnie, R. et al.; Abbott Laboratories, CHAD D377/AP6D, One Abbott Park Road, Abbott Park, IL 60064-3500 (US). (81) Designated States: CA, JP, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report.</i>
(54) Title: BUFFERED DIAPER RASH CREAM (57) Abstract <p>A buffered skin cream containing a linear polydimethylsiloxane polymer, a non-ionic emulsifier, aloe vera, mineral oil, sodium citrate, citric acid, a blend of propylene glycol, diazolidinyl urea, methyl paraben and propyl paraben, and water. The buffering capacity of the cream is provided through the incorporation of citric acid and sodium citrate in the composition. The buffering system results in the cream having a preferred pH in the range of about 4.5 to 6.0, and most preferably a pH of about 5.2 which neutralizes acidic and basic by-products of urine and fecal matter. The cream has a preferred viscosity in the range of 100,000-2,000,000 centipoise and a most preferred viscosity of about 250,000 to 1,000,000 centipoise. The cream is easily washed off with soap and water and is useful in the protection and treatment of diaper rash.</p>		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	GB	United Kingdom	MR	Mauritania
AU	Australia	GE	Georgia	MW	Malawi
BB	Barbados	GN	Guinea	NE	Niger
BE	Belgium	GR	Greece	NL	Netherlands
BF	Burkina Faso	HU	Hungary	NO	Norway
BG	Bulgaria	IE	Ireland	NZ	New Zealand
BJ	Benin	IT	Italy	PL	Poland
BR	Brazil	JP	Japan	PT	Portugal
BY	Belarus	KE	Kenya	RO	Romania
CA	Canada	KG	Kyrgyzstan	RU	Russian Federation
CF	Central African Republic	KP	Democratic People's Republic of Korea	SD	Sudan
CG	Congo	KR	Republic of Korea	SE	Sweden
CH	Switzerland	KZ	Kazakhstan	SI	Slovenia
CI	Côte d'Ivoire	LI	Liechtenstein	SK	Slovakia
CM	Cameroon	LK	Sri Lanka	SN	Senegal
CN	China	LU	Luxembourg	TD	Chad
CS	Czechoslovakia	LV	Latvia	TC	Togo
CZ	Czech Republic	MC	Monaco	TJ	Tajikistan
DE	Germany	MD	Republic of Moldova	TT	Trinidad and Tobago
DK	Denmark	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	US	United States of America
FI	Finland	MN	Mongolia	UZ	Uzbekistan
FR	France			VN	Viet Nam
GA	Gabon				

BUFFERED DIAPER RASH CREAM

TECHNICAL FIELD

The present invention relates generally to a buffered skin cream for use in connection with diaper rash.

BACKGROUND ART

One of the most common skin problems with infants relates to diaper rash, also known as diaper dermatitis. One study conducted with infants less than two years of age concluded that almost two-thirds of all infants suffer from diaper rash of some degree. Approximately 10% of all infants can have their diaper rash classified as being moderate, with another 5% of the infants having diaper rash which could be classified as severe.

The primary contributors to the development of diaper rash have long been thought to be infant urine and feces. For example, infants under two months of age can urinate up to 20 times per day. Thereafter, infants can urinate up to 8 times a day. In addition, infant defecation typically occurs several times a day.

It had been theorized that the breakdown of the urine to yield ammonia primarily contributed to the formation of diaper rash by increasing the alkalinity of the skin. However, more recent studies have concluded that the primary contributor to the development of diaper rash is feces. As opposed to the alkaline pH associated with urine, feces typically exhibits an acidic pH due to bile. In fact, studies have shown that diaper rash is more prominent in the presence of feces than in the presence of urine, thereby providing a plausible explanation for the problems with diaper rash associated with infants who have diarrhea or frequent stools.

Diaper rash may predispose an infant to irritation and infection. The two most common types of infection are those associated with yeast and bacteria. The most common yeast infection is caused by Candida albicans. Meanwhile, the most common bacterial infection is caused by Staphylococcus aureus.

Treatment for diaper rash involves removing the source of irritation, reducing the immediate skin reaction, relieving the discomfort and preventing secondary

infection and other complications. Frequent diaper changes and keeping the area as dry and clean as possible normally prove helpful. However, merely keeping the area clean and dry does not protect the irritated skin from the chemical irritation associated with the by-products of infant urine and feces.

In response to the problems associated with diaper rash, a number of products have been made available. The principle function of these products has been to act as a protectant, such that any affected area is protected against further direct contact with urine or feces. The most widely used protective ingredient has been zinc oxide. While many preparations contain zinc oxide in concentrations of approximately 10% by weight, some of the more popular brands have zinc oxide concentrations of approximately 40% by weight. Unless otherwise stated, the percentage concentrations of ingredients is understood to refer to percent by weight. Typically the zinc oxide is formulated with an oily substance such as petrolatum. Consequently, although such a diaper rash compound provides an effective protective layer, it is greasy, messy to apply, and not easily removed from the hands or the baby's bottom. Although removal can be affected with mineral oil, having to wash one's hands with mineral oil is inconvenient. Additionally, zinc oxide products have a distinctive smell due to their oil base, with this smell being offensive to some users of the product.

Most of the diaper rash products currently available are in the form of an ointment or a water-in-oil emulsion. The high viscosity associated with these products keeps the diaper rash product from being washed away by urine or feces. In many cases, the high viscosity is the result of the inclusion of zinc oxide. Thus, the typical anhydrous, hydrophobic ointment prevents urine or feces from coming into direct contact with the skin by their being repelled from the ointment surface. As such, the product acts as a barrier, inhibiting any penetration into the diaper rash product by any liquid.

An example of a diaper rash product is British Patent No. 1,357,731. That patent discloses a unique powder composition, which can be incorporated into a hydrophobic ointment. A buffer system is provided to buffer the composition at a pH of from 5.5 to 7.5, and preferably from 6 to 7. That patent discloses that a citric acid/sodium citrate buffering system does not have superior buffering capacity when compared with other buffering systems. This patent further discloses that "succinic acid/sodium succinate has 30% more buffering capacity than a citric acid/sodium citrate" buffer system. Thus this patent differs from the instant invention in that it claims use of a powder formulation having buffering capacity in the alkaline range of pH 5.5 to 7.5, and teaches away from the use of citric acid buffering system in view of the aforementioned comments related to the preferred use of a succinic acid buffer.

Another example of prior art is US Patent 4,556,560 issued on December 3, 1985 to Buckingham. This patent discloses and claims the use of lipase inhibiting agents, such as the water soluble metallic salts including zinc chloride, in the treatment of diaper rash. This patent purports to treat diaper rash by inhibiting the deleterious effects of the enzyme lipase action on the skin, said inhibition being achieved by incorporating an inhibitory agent of said lipase action into a barrier like carrier, said carrier having the characteristics of being relatively hydrophobic in nature thereby forming an effective barrier to the skin against urine and feces. The instant invention does not disclose nor claim use of lipase inhibitory agents. The instant invention is further distinguished from the Buckingham patent in that the present invention specifically claims use of a buffering system to neutralize acidic conditions. Buckingham neither teaches nor claims any buffering system. Further the instant invention is set apart from the Buckingham patent in the nature of the carrier material employed in the formation of the so-called skin barrier. In the case of Buckingham, specifically disclosed are water-in-oil types of emulsions. In contrast to Buckingham, the instant invention specifically discloses and claims use of oil-in-water type emulsions in the formation of the barrier material.

Yet another example of the prior art is US Patent No. 4,996,238 issued on February 26, 1991 to Matravers. This patent discloses and claims a skin protective composition exhibiting enhanced water repellency and skin conditioning effects and contains aliphatic waxes and hydrophobic silicones. Matravers' specifically discloses and claims the use of an admixture consisting of a fatty acid admixed with one or more hydrophobic silicones. This composition is devoid of water and further no buffering system is claimed. In contrast, the instant invention claims a water-based liquid product which contains a buffering system effective in acidic conditions.

Another example of the prior art is US Patent No. 4,904,524 issued on February 27, 1990 to Yoh. This patent discloses and claims the encapsulation and microbead formation and use thereof of the active silicon agent (Dimethicone) in the preparation of cloth wipes in the treatment of diaper rash. This patent specifically discloses the need for an elevated concentration of encapsulated beads containing the active agent at the surface of the wipe. The stability, presence and delivery of the active agent within the wipe is directly linked to, and dependent on the process used to form and adhere the encapsulated beads to the paper wipe. In contrast, the instant invention claims a water-based liquid product which contains a buffering system effective in acidic conditions. Further, the instant invention does not require, teach nor claim encapsulation of Dimethicone, one of the ingredients in the claimed composition.

Other studies, such as one published in The Practitioner, Vol. 210:824-828 (1973), discuss a boric acid/borax buffer system for use as a diaper rash product. However, studies conducted during the 1970's brought about concerns of boron toxicity such that products containing boric acid had to be reformulated thereby eliminating boric acid as an ingredient.

Still another approach to products containing anhydrous, hydrophobic zinc oxide was the incorporation into such products of alkoxylated ether/esters such as polypropyleneglycol myristyl ether propionate. Although this approach rendered the diaper rash products less greasy, it did not completely resolve the problem associated with the zinc oxide content.

It is thus apparent that a need exists for an improved diaper rash product which provides a safe system, which is easy to apply as well as easy to remove by simple cleaning agents such as soap and water.

DISCLOSURE OF THE INVENTION

There is disclosed a buffered skin cream comprising stearic acid, a linear polydimethylsiloxane polymer, a non-ionic emulsifier composed of a mixture of cetearyl alcohol and its ethoxylate, mineral oil, aloe vera, sodium citrate, citric acid, a naturally derived, non-ionic, water soluble polymer, a blend of propylene glycol, diazolidinyl urea, methyl paraben, and propyl paraben, and water. Preferably the sodium citrate and citric acid cooperate to form a buffering system having a pH in the range of between 4.0 and 6.5. More preferably the sodium citrate and citric acid cooperate to form a buffering system having a pH in the range of between 5.0 and 5.5. Most preferably the sodium citrate and citric acid cooperate to form a buffering system having a pH of 5.2.

In the buffered skin cream of this invention, the naturally derived, non-ionic water-soluble polymer preferably is nonoxynyl hydroxyethylcellulose. Additionally, the skin cream has a neutral olfactory sensation. The viscosity of the skin cream is in the range of between 100,000 centipoise and 2,000,000 centipoise. Additionally, the skin cream is soluble in soap and water. Furthermore, the stearic acid has a saponification value of between 197 and 200, and an iodine value of not more than 1. Still further, the mineral oil is a light mineral oil with a specific gravity of between 0.818 and 0.880.

There is also disclosed a buffered skin cream comprising stearic acid having a saponification value of between 197 and 200, and an iodine value of not more than 1, with the stearic acid also of a concentration of about 10% by weight, a linear polydimethylsiloxane polymer of a concentration of about 20% by weight, a

non-ionic emulsifier, said emulsifier being of a concentration of about 8% by weight, light mineral oil with a specific gravity of between 0.818 and 0.880 of a concentration of about 4% by weight, aloe vera of a concentration of about 1% by weight, sodium citrate of a concentration of about 3% by weight, citric acid of a concentration of about 0.5% by weight, water of a concentration of about 47% by weight, a naturally derived, non-ionic water soluble polymer of a concentration of about 0.5% by weight, and a blend of propylene glycol, diazolidinyl urea, methyl paraben, and propyl paraben, said blend of a concentration of about 1% by weight.

The sodium citrate and citric acid preferably will cooperate to form a buffering system having a pH in the range of between 4.0 and 6.5. More preferably the sodium citrate and citric acid cooperate to form a buffering system having a pH in the range of between 4.5 and 6.0. Most preferably sodium citrate and said citric acid cooperate to form a buffering system having a pH of between 5.0 and 5.5. Buffering capacity is independent of Dimethicone concentrations.

Additionally, the buffered skin cream preferably includes aloe vera and anhydrous lanolin.

One aspect of the present invention provides an effective, easy to apply and remove diaper rash cream having a buffering system to maintain the pH of the product at approximately the natural skin pH.

Other aspects and advantages of the instant invention will be apparent from the following descriptive examples and the appended claims.

DETAILED DESCRIPTION OF THE INVENTION

Specifically, the present invention is concerned with a buffered skin cream for use primarily in the treatment of diaper rash. The present invention could also be used in an attempt to prevent diaper rash by inhibiting contact with the skin of either feces or urine. The preventative aspect of the product occurs solely due to the buffering capacity and to the protectant included in the formulation of the cream.

The buffered diaper rash cream embodiments of this invention are comprised of an oil-in-water emulsion which incorporates a simple and safe buffering system. More specifically, the buffering system of the present invention is comprised of citric acid and sodium citrate. Although the buffering system is relatively simple, the system's capacity is sufficient to maintain the pH of the cream relatively close to the normal pH of skin, despite the addition of significant amounts of either, or both, alkaline and acidic materials, such as ammonia and hydrochloric acid.

Since the buffered cream embodiments of this invention are oil-in-water emulsions, the product can be easily removed from the skin or clothing by washing with soap and water. Additionally, the product does not leave a greasy feeling on the skin. Still further, in the preferred embodiment of the invention, no fragrance is added to the cream, such that the end-product has a neutral olfactory sensation. Importantly the diaper rash cream of this invention possess excellent protective qualities comparable to those associated with leading diaper rash treatment products, particularly the well known ointments.

In use, the diaper rash cream embodiment of this invention is spread on sufficiently thick over the affected area to allow a good coating of the area to be protected. The infant may then be diapered in either cloth or disposable diapers. When it becomes time to change the baby's diaper, the area can be cleaned, preferably with soap and water, and thereafter allowed to dry before reapplication of the diaper rash cream and re-diapering.

BEST MODE FOR CARRYING OUT THE INVENTION

A representative formula for the buffered diaper rash cream of the invention is set forth in Table 1.

TABLE 1 – BUFFERED DIAPER RASH CREAM

INGREDIENT	CONCENTRATION (Percent by Weight)
Non-ionic emulsifier composed of a mixture of cetearyl alcohol and its ethoxylate	8%
Linear polydimethylsiloxane polymer with an average kinematic viscosity of 12,500 centistokes	20%
Anhydrous Lanolin	14%
Light mineral oil with a specific gravity of between 0.818 and 0.880	6%
Stearic acid with a saponification value between 197–200 and an iodine value of not more than 1	8%
Aloe vera	2%
A blend of propylene glycol, diazolidinyl urea, methyl paraben and propyl paraben	1%
Sodium citrate	3%
Citric acid	0.25%
Naturally derived, non-ionic, water soluble polymer	0.5%
Purified water	37.5%

A skin cream according to this invention is prepared in the following manner. Turning to Table 1, the first five listed ingredients are combined and then heated to between 65–75°C, preferably to between 70–72°C. (Solution A). The water is then separately heated to between 65–75°C, and also preferably to between 70–72°C. As the water is heating the non-ionic water soluble polymer is added and the resultant solution agitated (Solution B).

When the temperatures of both liquids are in the desired range, they are combined. This is best achieved by slowly adding, with vigorous agitation, Solution B to Solution A. Care must be taken that the oil solution not begin to solidify at this time, so it may be easier to add the water solution to the oil solution. Preferably, once the solutions are combined, the temperature is maintained in the range of 65–75°C, preferably to between 70–72°C, and vigorous agitation continues for about 15–20 minutes.

The combined solution is then cooled. During cooling, the buffering system, consisting of sodium citrate and citric acid, is preferably first added. Finally, the aloe and blend of preservatives are added. However, this addition should occur when the temperature of the solution is less than 55°C. Water is then added to the achieve the desired volume and relative concentration of the individual components. The product will begin to thicken once its temperature is between 45–50°C.

In the preferred cream embodiment of the invention the first component, namely the non-ionic emulsifier is Promulgen D, is a blend of a fatty alcohol (cetearyl alcohol) and a polyethyleneglycol ether of cetaryl alcohol. Promulgen D is a product distributed by Amerchol Corporation, Edison, New Jersey, U.S.A. The linear polymer is the protectant associated with this invention. In one embodiment of the invention the protectant is Dow Corning 200 Fluid, 12,500 centistokes. This Dimethicone compound is a linear polydimethylsiloxane polymer which is not readily water soluble and has an average kinematic viscosity of 12,500 centistokes. It will be readily appreciated by those skilled in the art that other larger or smaller polydimethylsiloxane polymers can also be employed in the formulations of the instant invention. Such other polydimethylsiloxane polymers include Dimethicone having an average kinematic viscosity of 100 centistokes.

The lightweight mineral oil functions as an emollient in the preferred cream embodiment. An emollient serves to reduce the greasy feeling associated with use of Dimethicone. The stearic acid functions as a thickener. The blend of propylene glycol, diazolidinyl urea, methyl paraben and propyl paraben in the preferred embodiment of the invention is Germaben IIE, a preservative system. Germaben IIE is distributed by Sutton Laboratories of Chatham, New Jersey U.S.A.

Sodium citrate and citric acid, working in combination one with the other, constitute the buffering system of the instant invention. Finally, the naturally derived water soluble polymer in the preferred embodiment of the invention is Amercell HM-1500 a thickener comprising nonoxynyl hydroxyethylcellulose. Amercell 1500 is distributed by Amerchol Corporation of Edison, New Jersey, U.S.A.

Hydroxypropylmethylcellulose could also be utilized as a thickener in place of nonoxynyl hydroxyethylcellulose, however, the Amercell HM-1500 is a more effective thickener in the cream of this invention than is hydroxypropylmethylcellulose.

A representative range of the formula composition for the buffered diaper rash cream embodiment of the invention is set forth in Table 2.

TABLE 2 - Buffered Diaper Rash Cream

INGREDIENT (weight %)	CONCENTRATION RANGE		
	<u>Acceptable</u>	<u>Preferred</u>	<u>Most Preferred</u>
Non-ionic emulsifier**	3 - 11	5 - 10	7 - 9
Dimethicone, 12,500 cst	1 - 30	10 - 30	15 - 25
Stearic Acid	2 - 12	6 - 10	7 - 9
Mineral oil	2 - 9	4 - 8	5 - 7
Sodium citrate	1 - 8	1.5 - 6	2 - 4
Citric acid	0.1 - 1.0	0.15 - 0.75	0.2 - 0.5
Aloe Vera Gel	0 - 5	0 - 4	1 - 3
Anhydrous Lanolin	0 - 20	5 - 20	10 - 15
Preservative	0.2 - 3	0.2 - 2	0.5 - 1.5
Nonoxynyl-hydroxyethyl cellulose	0 - 2	0 - 1	0.4 - 0.6
Purified water	10 - 80	20 - 60	30 - 50

** Selected from the group of non-ionic emulsifiers consisting of polyoxyethylene sorbitan fatty acid esters, sorbitan fatty acid esters, polyoxyethylene alcohols and polyoxyethylene fatty ethers.

The buffered cream composition noted in Table 2, having a Dimethicone concentration in the range of about 1 - 30% by weight, has an acceptable viscosity and pH range of about 100,000 to 2,000,000 centipoise and about 4.0 to 6.5 respectively. These compositions will have a more preferred viscosity and pH range of about 150,000 - 1,500,000 centipoise and 4.5 - 6.0, respectively. The compositions will have a most preferred viscosity and pH in the range of about 250,000 - 1,000,000 centipoise and 5.0 - 5.5, respectively.

The expected method of preparation of the buffered diaper rash cream formulation was to add the sodium citrate and the citric acid to the water and heat the solution to between 70–75°C. The oil phase was then added at the same temperature and the product was agitated. Unexpectedly, no emulsification appeared to have occurred. Once agitation was stopped, the product separated into two distinct layers.

Thus, it was discovered that for an emulsified cream to be formed, the water phase had to be added to the water, with both liquids at between 70–75°C. Emulsification took place and cooling was started. At 50°C the blend of propylene glycol, diazolidinyl urea, methyl paraben and propyl paraben was added. At 43°C the citric acid was added. At 38°C the sodium citrate was added. At 30°C the agitation was stopped. The appearance of the product was good. Additionally, the pH was 5.2 and a viscosity of 200,000 centipoise was determined.

In the preferred buffered skin cream embodiment of the invention the linear polymer is the protectant associated with this invention. In a preferred embodiment of the invention the linear polydimethylsiloxane polymer protectant employed is Dow Corning 200 Fluid, 12,500 centistokes. This Dimethicone compound is not readily water soluble and has an average kinematic viscosity of 12,500 centistokes. (It will be readily appreciated by those skilled in the art that other larger or smaller linear polydimethylsiloxane polymers could also be used). The blend of propylene glycol, diazolidinyl urea, methyl paraben and propyl paraben in the preferred embodiment of the invention is Germaben IIE, a preservative system.

Preferably the pH for the buffered cream is between 4.0 and 6.5. More preferably the pH of the cream is between 5.0 and 5.5, and most preferably the pH is 5.2.

The invention will be better understood in view of the following examples, which are illustrative only and should not be construed as limiting the invention.

EXPERIMENTAL – DETERMINATION OF CREAM COMPOSITION

EXAMPLE 1 – CONTROL

The ingredients in Table 1 were combined, except that neither sodium citrate nor citric acid were added. The resultant cream is easy to apply and remove, however, when subjected to extremes in pH, tends to become more ammoniacal if a base is added, but if a strong acid is added then it tends to become very acidic.

EXAMPLE 2 – CONTROL

The ingredients of Table 1 were combined, except that boric acid and borate were substituted for the buffering system of the invention. The resultant cream raised concerns about boron toxicity, such that it would be unacceptable for use on infants based on current medical knowledge.

EXAMPLE 3 – CONTROL

The ingredients of Table 1 were combined, except that the naturally derived non-ionic, water soluble polymer was omitted. The resultant cream did not exhibit the proper viscosity. Additionally, increasing the concentration of stearic acid to obtain an acceptable viscosity resulted in the stearic acid having to be increased more than two-fold. Even then, the resultant cream did not possess the desirable properties of the cream associated with the invention.

EXAMPLE 4 – CONTROL

The ingredients of Table 1 were combined, except that stearic acid was omitted. Without the inclusion of stearic acid, the desired viscosity was not able to be obtained regardless of how much naturally derived, non-ionic, water soluble polymer, preferably nonoxynyl hydroxyethylcellulose, was added.

EXAMPLE 5 – INVENTION

The ingredients of Table 1 were combined as shown in Table 1. The resultant cream exhibited a pH of between 5 and 5.5, typically 5.2. Tests conducted with a Brookfield viscometer at spindle 4, 3 rpm, for two minutes disclosed a viscosity of 200,000 centipoise. The resultant diaper rash cream was acceptable for use on human skin. Under typical room temperature conditions the cream of this invention is a thick, viscous cream which is non-pourable.

EXAMPLE 6 – BUFFERING CAPACITY OF INVENTION

To establish the efficacy of the buffering system of this invention, several experiments were conducted. In the first two experiments a 300 ml. aqueous solution of 3% sodium citrate and 0.5% citric acid was prepared. In the first experiment, the results of which are set forth in Table 3, a 0.036% aqueous solution of HCl was prepared and titrated into the buffer solution with agitation. In the second experiment, the results of which are set forth in Table 4, a 0.06% aqueous solution of NH₃ was prepared and titrated into the buffer solution with agitation. In both cases, the pH was measured at frequent intervals.

TABLE 3 – BUFFERING IN PRESENCE OF ACID

<u>GRAMS OF HCl SOLUTION ADDED</u>	<u>pH</u>
0	5.49
4.4	5.42
9.6	5.41
14.3	5.40
19.5	5.39
24.7	5.38
32.4	5.37
38.8	5.38
43.8	5.37
49.3	5.37
55.4	5.35
63.6	5.35
67.3	5.35

TABLE 4 – BUFFERING IN PRESENCE OF BASE

<u>GRAMS OF NH3 SOLUTION ADDED</u>	<u>pH</u>
0	5.50
5.1	5.44
10.2	5.44
15.3	5.43
23.0	5.44
30.0	5.44
38.6	5.45
49.6	5.47
61.0	5.47
77.0	5.49

In the third experiment, 15 grams of the cream of the formulation of Table 1 were placed in a beaker. Measured amounts of a 0.06% aqueous solution of NH₃ were added and mixed with the cream for two minutes. The pH was measured at three time intervals after the mixing. The results are set forth below in Table 5.

TABLE 5 – BUFFERING OF INVENTION

<u>Grams of NH3 Solution Added</u>	<u>pH after 5 minutes</u>	<u>pH after 30 minutes</u>	<u>pH after 3 Hours</u>
8	5.39	5.32	5.27
12	5.63	5.51	5.35
16	6.08	5.71	5.35
NH3 Solution Control	10.49	10.48	10.09

The results of these three experiments show that the diaper rash cream of this invention is extremely effective in buffering the effects of acidic feces or alkaline urine.

EXAMPLE 7 – ABSORPTION TESTS

The diaper rash cream embodiment of this invention having the formulation of Table 1, as well as modified compositions having 5%, 10%, and 30% Dimethicone concentrations, was compared with Desitin which is a leading diaper rash ointment having zinc oxide as its protectant. (Desitin is distributed by the Consumer Health Care Division of Pfizer, Inc. of New York, New York, U.S.A.) In this test, for each sample tested, the first step was to weigh a clean, glass microscope slide ("original slide weight"). A coating of the sample to be tested was uniformly applied to one half of one side of the clean slide. The coated slide was then weighed ("original coated slide weight"). The coated slide then had its coated portion immersed in 100 ml. of purified water. The beaker with the partially immersed slide was then placed in a 400°C oven for 1 hour. After that time the slide was removed from the water and had its uncoated portions dried. The dried slide was then weighed, left at room temperature for 2 hours, and then weighed again ("final slide weight"). All samples were tested twice.

Percentage of absorption was determined by the following equation:

$$\% \text{ Absorption} = 100 \times \frac{\text{Final slide weight} - \text{original slide weight}}{\text{Original coated slide weight} - \text{original slide weight}}$$

The percentage of absorption indicates how much of the cream or ointment was removed by the water where "% absorption" is less than 100, or how much water was able to be absorbed as a percentage of the cream's weight where "% absorption" is greater than 100. In those cases, for example, a "% absorption" determination of 200 would mean that the cream was able to absorb its own weight in water, or in effect to double its weight due to apparent absorption.

As set forth below in Table 6, it will be noted that over time, while relatively little change occurred with respect to the weight of the ointment layer (in fact it lost some weight), the cream of this invention unexpectedly apparently absorbed the liquid into the cream as shown by the increase in weight.

TABLE 6 – ABSORPTION of LIQUID

<u>Formulations Tested</u>	<u>% Absorption</u>	
	<u>First Trial</u>	<u>Second Trial</u>
Diaper rash cream of this Invention – Table 1	216	214
Modified Table 1 cream – 5% Dimethicone	187	173
Modified Table 1 cream – 10% Dimethicone	186	198
Modified Table 1 cream – 30% Dimethicone	163	183
Leading Zinc Oxide ointment	98	98

The results from this experiment demonstrate a further unique aspect of the cream embodiment of this invention. Not only does the diaper rash cream of this invention counteract attempted dramatic shifts in pH due to its buffering capacity, but it also absorbs liquid into itself thereby minimizing the presence of alkaline or acidic solutions in actual contact with the skin.

The buffered diaper rash cream of this invention is effective in preventing diaper rash. It is also easy to use since it may be washed off with soap and water. The buffered diaper rash cream is aromatically and tactilely pleasing.

Additionally a variety of delivery systems may be used. For example, with respect to the cream, it may be applied directly to the skin, either by hand or via wipes. The cream preferably appears whitish in its dispenser, but rubs on translucent.

While the buffered diaper rash cream herein described constitute preferred embodiments of this invention, it is to be understood that the invention is not limited to the precise formulation and that changes may be made therein without departing from the scope of the invention which is defined in the appended claims.

CLAIMS:

1. A buffered skin cream having a viscosity of about 100,000 to 2,000,000 centipoise and a pH of about 4.0 to 6.5, said cream comprising:
 - (a) a linear polydimethylsiloxane polymer in a concentration by weight of about 1 to 30%;
 - (b) a non-ionic emulsifier in a concentration by weight of about 3 to 11%;
 - (c) sodium citrate in a concentration by weight of about 1 to 10%;
 - (d) citric acid in a concentration by weight of about 0.10 to 1.0%;
 - (e) a blend of propylene glycol, diazolidinyl urea, methyl paraben, and propyl paraben in a concentration by weight of about 0.2 to 3%;
 - (f) mineral oil in a concentration by weight of about 0 to 10%;
 - (g) stearic acid in a concentration by weight of about 2 to 12%;
 - (h) nonoxynylhydroxyethylcellulose in a concentration by weight of about 0 to 2%; and
 - (i) water in a concentration by weight of about 10 to 80%.
2. A buffered skin cream according to claim 1 wherein said sodium citrate and said citric acid cooperate to form a buffering system having a pH in the range of between about 4.0 and 6.5.
3. A buffered skin cream according to claim 2 wherein said sodium citrate and said citric acid cooperate to form a buffering system having a pH in the range of between about 4.5 and 6.0.
4. A buffered skin cream according to claim 2 wherein said sodium citrate and said citric acid cooperate to form a buffering system having a pH of about 5.0 and 5.5.
5. A buffered skin cream according to claim 1 wherein said skin cream is soluble in soap and water, said sodium citrate and said citric acid cooperating to form a buffering system having a pH in the range of between 4.0 and 6.5.
6. A buffered skin cream, according to claim 1 which includes an anhydrous lanolin in a concentration by weight of about 0 to 20%.
7. A buffered skin cream according to claim 1 which includes aloe vera in a concentration by weight of about 0 to 5%.
8. A buffered skin cream according to claim 6 which includes aloe vera in a concentration by weight of about 0 to 5%.

9. A buffered skin cream according to claim 1 wherein said cream is delivered to skin by means of a wipe, a diaper, or a dabber.
10. A buffered skin cream according to claim 1 having a viscosity of about 150,000 to 1,500,000 centipoise and a pH of about 4.5 to 6.0, wherein said linear polydimethylsiloxane polymer is of a concentration of about 10 to 30% by weight, said emulsifier is of a concentration of about 5 to 10% by weight, said sodium citrate is of a concentration of about 1.5 to 6% by weight, said citric acid is of a concentration of about 0.15 to 0.75% by weight, said mineral oil is of a concentration of about 4 to 8% by weight, said blend of propylene glycol, diazolidinyl urea, methyl paraben, and propyl paraben is of a concentration of about 0.2 to 2% by weight, said stearic acid is of a concentration of about 6 to 10% by weight, said nonoxynylhydroxyethylcellulose is of a concentration of about 0 to 1.0%, and said water is of a concentration of about 20 to 60% by weight.
11. A buffered skin cream according to claim 1 having a viscosity of about 250,000 to 1,000,000 centipoise and a pH of about 5.0 to 6.0, wherein said linear polydimethylsiloxane polymer is of a concentration of about 15 to 25% by weight, said emulsifier is of a concentration of about 7 to 9% by weight, said sodium citrate is of a concentration of about 2 to 4% by weight, said citric acid is of a concentration of about 0.2 to 0.5% by weight, said mineral oil is of a concentration of about 5 to 7% by weight, said blend of propylene glycol, diazolidinyl urea, methyl paraben, and propyl paraben is of a concentration of about 0.5 to 1.5% by weight, said stearic acid is of a concentration of about 7 to 9% by weight, said nonoxynylhydroxyethylcellulose is of a concentration of about 0.4 to 0.6%, and said water is of a concentration of about 30 to 50% by weight.
12. A buffered skin cream according to claim 9 which includes anhydrous lanolin of a concentration of about 0 to 20% by weight.
13. A buffered skin cream according to claim 12 which includes aloe vera of a concentration of about 0 to 5% by weight.
14. A buffered skin cream for use in the prevention and treatment of diaper rash, said skin cream being soluble in soap and water, and having a viscosity of about 100,000 to 2,000,000 centipoise, and having a buffering system with a pH in the range of between 4.0 and 6.5, said buffering system comprising sodium citrate and citric acid.

15. A buffered skin cream according to claim 14 wherein said skin cream comprises:

- (a) a linear polydimethylsiloxane polymer in a concentration by weight of about 1 to 30%;
- (b) a non-ionic emulsifier in a concentration by weight of about 3 to 11%;
- (c) sodium citrate in a concentration by weight of about 1 to 10%;
- (d) citric acid in a concentration by weight of about 0.10 to 1.0%;
- (e) a blend of propylene glycol, diazolidinyl urea, methyl paraben, and propyl paraben in a concentration by weight of about 0.2 to 3%;
- (f) mineral oil in a concentration by weight of about 0 to 10%;
- (g) stearic acid in a concentration by weight of about 2 to 12%;
- (h) nonoxynylhydroxyethylcellulose in a concentration by weight of about 0 to 2%; and
- (i) water in a concentration by weight of about 10 to 80%.

16. A buffered skin cream according to claim 14 wherein said skin cream has a viscosity of about 150,000 to 1,500,000 centipoise and a pH of about 4.5 to 6.0, comprising:

- (a) a linear polydimethylsiloxane polymer in a concentration by weight of about 10 to 30%;
- (b) a non-ionic emulsifier in a concentration by weight of about 5 to 10%;
- (c) sodium citrate in a concentration by weight of about 1.5 to 6%;
- (d) citric acid in a concentration by weight of about 0.15 to 0.75%;
- (e) a blend of propylene glycol, diazolidinyl urea, methyl paraben, and propyl paraben in a concentration by weight of about 0.2 to 3%;
- (f) mineral oil in a concentration by weight of about 4 to 8%;
- (g) stearic acid in a concentration by weight of about 6 to 10%;
- (h) nonoxynylhydroxyethylcellulose in a concentration by weight of about 0 to 1%; and
- (i) water in a concentration by weight of about 20 to 60%.

17. A buffered skin cream according to claim 14 having a viscosity of about 250,000 to 1,000,000 centipoise and a pH of about 5.0 to 5.5, comprising:
- (a) a linear polydimethylsiloxane polymer in a concentration by weight of about 15 to 25%;
 - (b) a non-ionic emulsifier in a concentration by weight of about 7 to 9%;
 - (c) sodium citrate in a concentration by weight of about 2 to 4%;
 - (d) citric acid in a concentration by weight of about 0.2 to 0.5%;
 - (e) a blend of propylene glycol, diazolidinyl urea, methyl paraben, and propyl paraben in a concentration by weight of about 0.5 to 1.5%;
 - (f) mineral oil in a concentration by weight of about 5 to 7%;
 - (g) stearic acid in a concentration by weight of about 7 to 9%;
 - (h) nonoxynylhydroxyethylcellulose in a concentration by weight of about 0.4 to 0.6%; and
 - (i) water in a concentration by weight of about 30 to 50%.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US93/09869

A. CLASSIFICATION OF SUBJECT MATTER																				
IPC(5) : A61K 31/74 US CL : 424/78.03; 514/865 According to International Patent Classification (IPC) or to both national classification and IPC																				
B. FIELDS SEARCHED																				
Minimum documentation searched (classification system followed by classification symbols) U.S. : 424/401, 78/03; 514/865																				
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched																				
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) APS Search terms citric acid, sodium citrate, diaper rash, siloxane, paraben, stearic acid																				
C. DOCUMENTS CONSIDERED TO BE RELEVANT																				
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.																		
<u>Y</u> X	US, A, 4,536,399 (FLYNN ET AL) 20 AUGUST 1985; Columns 1-4.	<u>1-13, 15, 16</u> 14																		
Y	US, A, 4,904,524 (YOH) 27 FEBRUARY 1990, Columns 3-6.	1-16																		
A	US, A, 4,855,129 (STEINBACH) 08 AUGUST 1989, Columns 1-2.	1-16																		
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.																				
<table border="0"> <tr> <td colspan="2">* Special categories of cited documents:</td> <td></td> </tr> <tr> <td>*A*</td> <td>document defining the general state of the art which is not considered to be part of particular relevance</td> <td>*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</td> </tr> <tr> <td>*E*</td> <td>earliest document published on or after the international filing date</td> <td>*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</td> </tr> <tr> <td>*L*</td> <td>document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</td> <td>*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</td> </tr> <tr> <td>*O*</td> <td>document referring to an oral disclosure, use, exhibition or other means</td> <td></td> </tr> <tr> <td>*P*</td> <td>document published prior to the international filing date but later than the priority date claimed</td> <td>*A* document member of the same patent family</td> </tr> </table>			* Special categories of cited documents:			*A*	document defining the general state of the art which is not considered to be part of particular relevance	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention	*E*	earliest document published on or after the international filing date	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone	*L*	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art	*O*	document referring to an oral disclosure, use, exhibition or other means		*P*	document published prior to the international filing date but later than the priority date claimed	*A* document member of the same patent family
* Special categories of cited documents:																				
A	document defining the general state of the art which is not considered to be part of particular relevance	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention																		
E	earliest document published on or after the international filing date	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone																		
L	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art																		
O	document referring to an oral disclosure, use, exhibition or other means																			
P	document published prior to the international filing date but later than the priority date claimed	*A* document member of the same patent family																		
Date of the actual completion of the international search 02 DECEMBER 1993		Date of mailing of the international search report 04 FEB 1994																		
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. NOT APPLICABLE		Authorized officer THURMAN K. PAGE Telephone No. (703) 308-2351																		